52 Pain and Sensory Perversions

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Definition

Although pain is the most common symptom that brings a patient to the physician, it is impossible to give a precise definition, since only the individual suffering the pain can perceive and describe it. In general, pain is an uncomfortable sensory experience with both physiochemical and affective components. It serves to warn the individual of either physical or psychological damage. The clinician's duty is to discover and treat the source of the pain as well as to treat the pain itself.

In patients with sensory perversions, the sensory system is disordered; sensations may be diminished, increased, or distorted. Diminution or loss of pain sensation is termed *hypoalgesia* or *analgesia*. *Hyperpathia* indicates a lowered threshold for painful sensation. Stimuli that are usually nonpainful can cause pain (e.g., sunburn). Nervous system damage is characteristic in this condition. *Paresthesias* are spontaneous painful discharges (e.g., the burning sensation of diabetic neuropathy). *Causalgias* can be defined as a combination of hyperpathias and paresthesias.

Technique

Since pain is a subjective experience, an accurate history is essential. The most critical points in a "pain" history can be found in the mnemonic "P,Q,R,S,T."

P—*Provocative, palliative factors.* The examiner should be able to elicit factors that initiate or exacerbate the pain as well as factors that result in total or partial relief.

Q—*Quality.* There are three major qualities of pain: sharp, burning, and aching. Although there is considerable overlap, the first two are more characteristic of superficial pain and the last more characteristic of visceral pain.

R—*Region.* The examiner can help the patient to localize the pain with techniques such as having him outline the painful area with one finger. This can help localize the pain to a particular organ system or help determine if the pain is radiating to or from another organ system.

S—*Severity.* Although this is largely subjective, it is useful to know to what degree the patient views the pain as threatening or disabling. This can be accomplished by direct questioning or by having the patient compare the severity of the pain to a more common type of pain, such as a sprained ankle or minor burn.

T—*Temporal relationships.* The examiner should determine the time of onset of the pain and of its development, the number of times the pain has been experienced, and the duration of the pain. It is also important to note whether the pain is intermittent, associated with pain-free intervals, or chronic with exacerbations and remissions of the pain.

When the above historic information has been obtained, the examiner will usually have sufficient information to begin to develop a differential diagnosis. Although the features mentioned appear to be most applicable to episodes of acute pain, such as the pain associated with trauma or angina pectoris, they can be equally useful in patients with chronic pain or with sensory perversions.

Although patients with acute pain syndromes can easily relate factors that aggravate or relieve their discomfort, patients with chronic pain can seldom be exact about these factors. The quality of the discomfort in chronic pain is ill defined. The region of the pain is equally ill defined. It usually cannot be explained on known anatomic or physiologic grounds. The severity is almost always disabling, and the temporal characteristics are vague. Therefore, the inability of the patient to relate positive features regarding the pain can be useful in defining a patient with a chronic pain syndrome.

Patients with sensory perversions have nervous system damage and may give a history that is suggestive of a chronic pain syndrome. Although components of their history may not be as clear as those of the acute pain syndromes, they take on increased clarity when known physiologic mechanisms are invoked. An example would be the painful paresthesias associated with diabetes mellitus. Although provocative and palliative factors are ill defined, the burning and tingling quality is characteristic. When considered as a known complication of diabetes mellitus, the severity and temporal relationships are much more easily explained.

Basic Science

The sensation of pain is subserved by a complex network of peripheral and visceral nerves, the spinal cord, and the brain. Sensory neurons have either small (5 μ) myelinated fibers (A-delta) that conduct impulses rapidly (35 m/sec) or small (2 μ) unmyelinated fibers (C fibers) that conduct impulses more slowly (0.5 m/sec). The presence of these two types of fibers can explain the occurrence of "double pain," an initial sharp, well-localized pain mediated by the myelinated (A-delta) fibers followed by a poorly localized, aching pain mediated by the slower unmyelinated C fibers. These fibers are termed *polymodal nociceptors*, since they can be stimulated by several factors including temperature, mechanical deformation, and chemical mediators of inflammation. Polymodal nociceptors show increased activity and a decreased firing threshold with repeated activation, unlike most sensory receptors, which fatigue with repeated firing.

The primary afferent nociceptor is activated by a noxious stimulus. The message is transmitted over the small-diameter axons where they enter the spinal cord via both the

dorsal and ventral spinal roots. Cells in the spinal cord are then activated, and the signal is transmitted to the brainstem, thalamus, and cortex where modulating factors occur and where the conscious perception of pain takes place.

Pain transmission is subject to several modulating factors within the nervous system. These include the synergistic effects of the products of inflammation, the inhibiting effects of large-diameter nonnociceptive afferent fibers, and chemical modulation by catecholamines, substance P, serotonin, and the endorphins.

Combinations of chemical mediators of inflammation can have a synergistic effect in increasing the nociceptor activity of the peripheral nerves. Catecholamines can also be involved in the modulation of the primary afferent nociceptors. Although the mechanism by which the catecholamines influence pain transmission is not clear, it is hypothesized that there may be increased numbers of alpha-adrenergic receptors on injured C fibers and that increased activity results in a corresponding increase in the pain sensation.

Substance P is a neurotransmitter located in the polymodal nociceptors. Any stimulus strong enough to activate the C fibers also elicits the release of substance P into the cerebrospinal fluid. In experimental models, depletion of substance P from a polymodal nociceptor results in analgesia to noxious stimuli in the area subserved by the treated nerve.

Associated with the small-diameter nociceptive fibers are large-diameter nonnociceptive afferent fibers. These fibers were first postulated by Head in the early part of this century when he proposed the concept that peripheral sensation is composed of two distinct components. He termed these components epicritic, which mediate fine discrimination, and protopathic, which mediate noxious sensation. Conscious sensation results from a balance of the two. In 1965, Melzack and Wall proposed a gate-control theory of pain perception. Although the "gate" is not completely understood, the large-diameter fibers have a lower threshold for stimulation and can inhibit stimulation of the C-fiber nociceptors when they are activated.

The most significant findings in recent years regarding endogenous mediation of pain have been the discovery of opiate receptors in the brain and of endogenous morphine-like compounds, the endorphins. Although naturally occurring opioids have been known for centuries to be potent analgesics, only relatively recently have opioid compounds been synthesized. Shortly thereafter it was noted that some of these compounds were capable of antagonizing the effects of the opioids. From this observation developed the theory that there are two classes of compounds, agonists and antagonists, which compete for a binding site in the brain. By the mid-1970s, opioid receptors were identified, followed by the discovery of the first two endorphins, leucine and methionine enkephalin.

Recent work has shown that analgesia may be caused by stimulation of certain areas of the brain, such as the periaqueductal gray area. These areas of the brain also have high concentrations of endorphins. It is also theorized that there are at least three types of opiate receptors: mu, delta, and kappa. This information may help explain differing potencies and side effects of the opioid analgesics and help explain differing perceptions of pain.

Serotonin is a neurotransmitter that is involved with depression and plays a role in the modulation of pain. Descending pathways terminate on the spinal cord in areas close to spinal cord cells that are responsive to painful stimuli. There is a high concentration of serotonin in these terminal axons and stimulation of these cells inhibits the pain-responsive cells and, therefore, pain transmission.

Clinical Significance

The acute pain syndromes tend to have clear etiologies and respond readily to appropriate therapy. Chronic pain serves less of a warning function and becomes part of the patient's life. Chronic pain syndromes can be divided into three categories: (1) those associated with clinically significant structural disease (e.g., rheumatoid arthritis, cancer pain); (2) those associated with a history of structural disease but with psychological factors that predispose to physiologic alterations, such as muscle spasm in chronic lower back pain; (3) those with no anatomic or physiologic basis for the patient's complaints, exemplified by the somatoform disorders. The time frame for development of chronic pain is not exact.

In patients with acute pain syndromes or those with chronic pain related to chronic metabolic or structural changes, such as terminal cancer, an understanding of pain physiology can help the physician develop effective pain management techniques.

Acute Pain Syndromes

Treatment is most effective if transmission of pain can be blocked close to the stimulus. When possible, the first step in treating pain should be to remove the pathologic lesion initiating the pain. The next step should be to eliminate or modify the chemical mediators involved with the primary afferent nociceptors. The nonsteroidal anti-inflammatory drugs (NSAIDs) are the primary tools clinically available. These agents work by blocking the metabolism of arachidonic acid. When given before a noxious stimulus, they can block the generation of impulses in the nociceptors. If the stimulus is already present, they have no effect on the ongoing activity of the nociceptor. This explains why the continuous use of these drugs gives more effective pain relief than does occasional use, as is clearly seen in chronic inflammatory conditions, such as rheumatoid arthritis. Attempts to utilize other substances, such as antihistamine agents, to block specific chemical mediators of inflammation have not been effective.

Another effective approach in acute pain management is to lower the concentration of the chemical mediators. This is exemplified by application of cold after trauma.

If the inciting lesion cannot be removed and if interference with the chemical mediators is not satisfactory, local anesthetics may be considered as a temporary measure. They act by blocking conduction along the nociceptor fibers. In addition to being useful in pain control, local anesthetics also help to localize the pain. For example, if pain is not relieved by a local anesthetic, it may be referred from another area.

When the physician takes into account the pain-modulating factors, other pain-control measures become apparent. Since catecholamines can increase the sensation of pain, chemical and surgical sympathectomies are useful in certain situations, such as sympathetic dystrophy or causalgia. Efforts are being made to formulate specific substance P antagonists. This work promises to provide new agents to add to our pain relief armamentarium.

The gate theory of Malzack and Wall offers an explanation as to why transcutaneous electrical nerve stimulation (TENS) is effective. When the large-diameter non-nociceptive fibers are stimulated, the nonpainful impulse interferes with transmission of painful impulses along the primary afferent nociceptors. Since the non-nociceptive fibers have a lower threshold of stimulation, TENS units can selectively activate these fibers. These units are most effective in self-limited acute pain syndromes.

Other pain syndromes, such as some forms of headache, respond to use of the serotoninergic antidepressant amitriptyline. This agent increases the concentration of serotonin in the synaptic cleft and presumably has an inhibiting function on pain signal transmission.

More effective use of the narcotic analgesic agents can be made with the understanding of the opiate receptors and the endorphins. The benefits and limitations of therapy with placebos can be better understood, since their effectiveness involves the endogenous opioid system and endorphins. A positive placebo response involves stimulation of the endogenous opioid system. Although placebos have distinct limitations, the positive response that some patients achieve with lower than expected doses of analgesics probably involves the endogenous opioid system. Further research into utilizing this response for pain relief is being undertaken.

Chronic Pain Syndromes

Patients with the diagnosis of chronic pain syndrome, somatization disorder, or hypochondriacal disorder do not have detectable anatomic or physiologic derangements to explain their discomfort. Although treatment plans cannot be made using the principles outlined above, the physician needs to be aware of these patients since they constitute a significant percentage of any physician's practice.

Many of these patients will have some form of depression. Depression is emotional pain and is a complex phenomenon with biological, psychological, and social components. Emotional maturity is required to accurately recognize and accurately report emotional pain, but development of this maturity is often blunted in these patients. Since the source is emotional, their physical complaints cannot be explained on known physiologic grounds.

Some of these patients will respond to antidepressant pharmacotherapy. Others can best be managed with the help of a pain-control center. All will have a maximum response if a warm and caring relationship can be developed with a physician. At the least, these patients can be helped to improve their functional abilities and be more satisfied with life in spite of their pain.

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